

Full Text PA-97-060

EXPLORATORY GRANTS FOR MULTIDISCIPLINARY CLINICAL STUDIES OF SARCOPENIA

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THIS PROGRAM ANNOUNCEMENT IS A REVISION OF THE PA APPEARING IN THE MAY 9 ISSUE OF THE NIH GUIDE. THIS REVISION ADDS THE NIAMS AS A SPONSORING INSTITUTE OF THIS PROGRAM ANNOUNCEMENT.

PURPOSE

The National Institute on Aging (NIA) invites exploratory research grant (R21) applications for multidisciplinary, clinical studies on the mechanisms underlying the physical functional consequences of sarcopenia in older persons. This NIA exploratory grants program is intended to facilitate new collaborative efforts in the development of novel scientific hypotheses on the causes of changes in skeletal muscle morphology and/or metabolism which lead to physical disabilities in old age, by providing research support for the appropriate pilot/feasibility studies to refine these hypotheses. Multidisciplinary approaches may include collaborations between various types of clinical research expertise (e.g., epidemiology, geriatrics, rehabilitation medicine, biomechanics, exercise physiology), or between basic and clinical researchers, with or without previous aging research experience.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This program announcement (PA), Exploratory Grants for Multidisciplinary Clinical Studies of Sarcopenia, is related to the priority areas of chronic diseases and disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No.017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-512-1800).

ELIGIBILITY REQUIREMENTS

Applications for exploratory (R21) research grants may be submitted by foreign and domestic non-profit and for-profit, public and private, institutions such as a university, college, hospital, laboratory, units of State and local government; and eligible agencies of the Federal government. Applications may include collaborative arrangements between scientists from a single institution or multiple institutions. Simultaneous submissions of the same research project as both an exploratory grant and a regular research grant (RO1) will not be allowed.

Racial/ethnic minority individuals, women and persons with disabilities are encouraged to apply as Principal Investigators.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC Program Director or Principal Investigator should be included with the application.

MECHANISM OF SUPPORT

This program will use the NIH exploratory grant (R21) mechanism. Applicants may request up to \$100,000 per year in direct costs, exclusive of indirect costs for any collaborating institutions. Funds may be included to support travel for the collaborators and/or the purchase of equipment, as justified by the needs of the proposed research. Because the nature and the scope of the research proposed in response to this PA may vary, it is anticipated that the size of awards will vary as well. The total project period for an application submitted in response to this PA may not

exceed two years. These grants are non-renewable and continuation of projects developed under this program will be through the traditional unsolicited grants program.

RESEARCH OBJECTIVES

Background

The physical functional consequences of sarcopenia in the elderly include mobility problems, falls and an increased risk for physical functional dependence. Numerous studies have attributed the inability of older persons to perform various tasks to a decline in muscle function (e.g., loss of strength, decreased muscle power), but there is a paucity of clinical information about the mechanisms leading to muscle dysfunction in old age. In the meantime, various animal models and in vitro systems developed to study specific alterations in muscle quality suggest that factors such as age-associated changes in muscle contractility, satellite cell function, innervation/denervation and myofibrillar protein turnover could play a role in muscle dysfunction. From a clinical perspective, it has been difficult to interpret the animal and in vitro data since very few clinical studies have attempted to bridge the gap between these mechanistic data and the clinical assessment of the physical functional status of the elderly. Given the wide variety of age-related changes in muscle quality, which are thought to contribute to physical functional problems in old age, multidisciplinary approaches will be needed to better define the relationship between sarcopenia and deficits in physical performance.

To initiate discussions on promising multidisciplinary approaches and novel methodologies available for elucidating the alterations in muscle quality underlying deficits in physical performance in the elderly, the NIA convened the workshop, "Sarcopenia and Physical Performance in Old Age" on July 9-10, 1996. Diverse research backgrounds (e.g., aging and non-aging research expertise, clinical and basic science investigators, skeletal muscle biology, exercise physiology, neurology, statistics) were represented by the workshop participants in the scientific sessions, which included: 1) Specific Study Design Considerations, 2) Muscle Function and Physical Performance and 3) Muscle Function and Pathophysiology. Abstracts of the presentations and a summary of the workshop recommendations will be published as a supplement to *Muscle & Nerve*, in early 1997. The main goals of the workshop were to: 1) stimulate more clinical studies of the relationship between changes in muscle function and specific limitations in physical performance, 2) encourage a focus on disabled and frail elderly populations, as well as minorities, 3) promote more comprehensive evaluations of muscle quality in clinical studies, particularly through the use of non-invasive measures of muscle properties, and 4) explore the possibility of more detailed analysis of human muscle biopsy samples through

the adaptation of in vitro methods commonly used in animal studies. The NIA exploratory grants program is intended to encourage collaborations between various scientific disciplines to operationalize the workshop goals into future clinical studies of sarcopenia and its physical functional consequences. It is anticipated that the pilot/feasibility studies supported by the NIA exploratory grants program will constitute the scientific framework for larger, innovative clinical studies of the mechanisms underlying disabilities related to sarcopenia in old age.

Objectives

This initiative will provide research support to explore novel multidisciplinary approaches for understanding the clinical relevance of changes in skeletal muscle (i.e., at the cellular or organ level) in the context of the physical functional status of an older individual and, vice versa.

Applications submitted in response to this PA must address the mechanistic aspects (i.e., alterations in skeletal muscle mass/quality with aging) of physical disabilities associated with sarcopenia. Topics of interest include, but are not limited to:

- o Quantitative assessment of muscle quality and function associated with various levels of physical performance (e.g., relationship between muscle fatigue and ability/inability to climb stairs; rate of muscle force development and ability to react to "time-critical" situations)
- o Pilot studies of the clinical application of basic research findings
- o Correlative data between non-invasive measures of muscle quality and measures from animal or in vitro experimental measures of muscle properties (e.g., blood supply, contractility)
- o Feasibility studies required to "translate" findings from small-scale mechanistic studies to population-based studies of the functional consequences of sarcopenia
- o Potential ethnic or gender differences in the determinants (i.e., of changes in muscle quality/function) of physical disabilities associated with sarcopenia
- o Impact of chronic diseases on muscle function/quality and its physical functional consequences in old age

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 5/95) and will be accepted at the February 1, June 1 and October 1 application deadlines as indicated in the application kit. Applications kits are available at most institutional offices of sponsored research and may be obtained from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301-435-0714, Email: ASKNIH@odrockm1.od.nih.gov. The title and number of the program announcement must be typed in section 2 on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

DIVISION OF RESEARCH GRANTS
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817 (for express/courier service)

REVIEW CONSIDERATIONS

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications that are complete will be evaluated for scientific and technical merit by study sections of the Division of Research Grants, NIH, in accordance with the standard NIH peer review procedures. As part of the initial merit review, all applications deemed to have the highest scientific merit, generally the top half of the applications under review will be discussed, assigned a priority score and receive a second level of review by the appropriate national advisory council.

Review Criteria

- o Scientific, technical, or medical significance and originality of the proposed research;
- o Appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;
- o Qualifications and research experience of the Principal Investigator, collaborators and key research personnel, particularly but not exclusively, in the area of proposed research;
- o Availability of adequate facilities, general environment for the conduct of the proposed research and feasibility of the collaborative arrangements;
- o Appropriateness of the proposed budget and duration in relation to the proposed research;
- o Adequacy of plans to include both genders and minorities and their subgroups as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

The initial review group will also examine the provisions for the protection of human and animal subjects, and the safety of the research environment.

AWARDS CRITERIA

Scored applications will compete for available funds with all other scored applications assigned to that Institute/Center. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review;
- o Availability of funds; and

- o Program balance among research areas of the program announcement.

INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applications is welcome.

Direct inquiries regarding programmatic issues to:

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Muscle Biology and Musculoskeletal Fitness Program Director
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Natcher Building, Room 5AS 49E
Bethesda, MD 20892-6500
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FAX: (301) 480-4543
Email: lymnr@ep.niams.nih.gov

Direct inquiries regarding fiscal matters to:

Mr. Joseph Ellis
Grants and Contracts Management Office
National Institute on Aging
7201 Wisconsin Avenue, Suite 2N212, MSC 9205
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Telephone: (301) 496-1472

FAX: (301) 402-3672

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AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.866, Aging Research and No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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